DEPARTMENT OF HEALTH AND HUMAN SERVICES

DMB

Food and Drug Administration

21 CFR Parts 20, 510, 514, and 516

[Docket No. 2005N–0329]

RIN 0910–AF60

Designation of New Animal Drugs for Minor Uses or Minor Species

AGENCY: Food and Drug Administration, HHS.

ACTION: Proposed rule.

SUMMARY: The Minor Use and Minor Species Animal Health Act of 2004 (MUMS act) amended the Federal Food, Drug, and Cosmetic Act (the act) to establish new regulatory procedures that provide incentives intended to make more drugs legally available to veterinarians and animal owners for the treatment of minor animal species and uncommon diseases in major animal species. At this time, FDA is issuing proposed regulations to implement the act. These regulations propose procedures for designating a new animal drug as a minor use or minor species drug. Such designation establishes eligibility for the incentives provided by the MUMS act.

DATES: Submit written or electronic comments on this document by [*insert date 75 days after date of publication in the* **Federal Register**]. Submit comments on the information collection provisions by [*insert date 30 days after date of publication in the* **Federal Register**].

ADDRESSES: You may submit comments, identified by Docket No. 2005N–0329 and/or RIN number 0910–AF60, by any of the following methods:

cv053 2005N-0329

NPR 1

Electronic Submissions

Submit electronic comments in the following ways:

- Federal eRulemaking Portal: *http://www.regulations.gov*. Follow the instructions for submitting comments.
- Agency Web site: *http://www.fda.gov/dockets/ecomments*. Follow the instructions for submitting comments on the agency Web site.

Written Submissions

Submit written submissions in the following ways:

- FAX: 301-827-6870.
- Mail/Hand delivery/Courier (for paper, disk, or CD–ROM submissions): Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

To ensure timely processing of electronic comments, FDA is no longer accepting comments submitted to the agency by e-mail. FDA encourages you to continue to submit electronic comments by using the Federal eRulemaking Portal and agency Web site, as described in the *Electronic Submissions* portion of this paragraph.

Instructions: All submissions received must include the agency name and docket number or regulatory information number for this rulemaking. All comments received may be posted without change to *http://www.fda.gov/ohrms/dockets/default.htm*, including any personal information provided. For detailed instructions on submitting comments and additional information on the rulemaking process, see the "Comments" heading of the **SUPPLEMENTARY INFORMATION** section of this document.

Docket: For access to the docket to read background documents or comments received, go to *http://www.fda.gov/ohrms/dockets/default.htm* and

insert the docket number found in brackets in the heading of this document, into the "Search" box and follow the prompts and/or go to the Division of Dockets Management, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Andrew Beaulieu, Center for Veterinary Medicine (HFV–50), Food and Drug Administration, 7519 Standish Pl., Rockville, MD 20855, 240–276–9090, e-mail: *Andrew.Beaulieu@fda.gov.*

SUPPLEMENTARY INFORMATION:

I. Background

In enacting the MUMS act (Public Law 108–282), Congress sought to encourage the development of animal drugs that are currently unavailable to minor species (species other than cattle, horses, swine, chickens, turkeys, dogs, and cats) in the United States or to major species afflicted with uncommon diseases or conditions (minor uses). Congress recognized that the markets for drugs intended to treat these species, diseases, or conditions are so small that there are often insufficient economic incentives to motivate sponsors to develop data to support approvals. Further, Congress recognized that some minor species populations are too small or their management systems too diverse to make it practical to conduct traditional studies to demonstrate safety and effectiveness of these animal drugs. As a result of these limitations, sponsors have generally not been willing or able to collect data to support legal marketing of drugs for these species, diseases, or conditions. Consequently, Congress enacted the MUMS act, which amended the Federal Food, Drug, and Cosmetic Act (the act) to provide incentives to develop new animal drugs for minor species and minor uses, while still ensuring appropriate safeguards for animal and human health.

At this time, FDA is issuing proposed regulations to implement section 573 of the act (21 U.S.C. 360ccc-2). These regulations propose procedures for designating a new animal drug as a minor use or minor species drug. Such designation provides eligibility for certain incentives established by the MUMS act, including exclusive marketing rights associated with the conditional approval or approval of designated new animal drugs and for grants to support designated new animal drug development. In accordance with section 573 of the act, these proposed regulations provide for designation of a new animal drug to be granted only when the drug is intended for a minor use or use in a minor species and only when the same new animal drug, in the same dosage form, for the same intended use is not already approved under section 512 of the act (21 U.S.C. 360b), conditionally approved under section 571 of the act (21 U.S.C. 360ccc), or designated under section 573 of the act at the time that a sponsor requests designation.

The incentives in the MUMS act and these proposed regulations are modeled on those provided by the human orphan drug program. These incentives include the following: (1) Eligibility for grants and contracts to defray the costs of qualified safety and effectiveness testing expenses and manufacturing expenses incurred in the development of designated new animal drugs and (2) a 7-year period of exclusive marketing rights to enable sponsors to recover costs of drug development without competition. Marketing exclusivity for nondesignated drugs is limited to 3 or 5 years of protection from generic copying (section 512(c)(2)(F) of the act). The exclusive marketing rights for designated drugs provide protection from generic copying and from approval of another pioneer application for the same drug, in the same dosage form, for the same intended use.

Other major incentives of the MUMS act include the following: (1) Conditional approval, which is established by section 571 of the act and provides for animal drug marketing after all safety and manufacturing components of a new animal drug approval have met the standards of section 512 of the act (for the effectiveness component, a reasonable expectation of effectiveness must be established, after which sponsors have up to 5 years to complete the demonstration of effectiveness by the standards of section 512 of the act and achieve a full approval) and (2) indexing, which is established by section 572 of the act (21 U.S.C. 360ccc-1) and provides for legal marketing of unapproved new animal drugs through an integrated process of agency and expert panel review of drugs intended only for use in minor species. Regulations to implement these provisions of the MUMS act will be proposed in the future.

II. Proposed Regulations

A. Definitions (Proposed §§ 516.3 and 516.13)

Under the MUMS act, there are two key factors in determining the eligibility of a new animal drug for designation: (1) The new animal drug must be intended for minor use or use in a minor species and (2) the new animal drug must not be the same drug, in the same dosage form, and for the same intended use as an animal drug already designated, conditionally approved, or approved. The agency is proposing definitions for terms or phrases relevant to the proposed regulations. Discussion regarding key definitions follows.

1. Minor Species

The MUMS act defines minor species as animals other than humans that are not major species. The MUMS act defines major species as cattle, horses, swine, chickens, turkeys, dogs, and cats, along with any species the Secretary

of Health and Human Services adds to this definition by regulation (see section 201(nn) and (oo) of the act (21 U.S.C. 321 (nn) and (oo)).) The proposed rule includes these definitions for "major species" and "minor species" in proposed § 516.3(b)(5) and (b)(6).

2. Minor Use

The MUMS act defines "minor use" to mean "the intended use of a drug in a major species for an indication that occurs infrequently and in only a small number of animals or in limited geographical areas and in only a small number of animals annually" (section 201(pp) of the act).

With respect to the definition of minor use, the Senate report (S. Rept. 108–226) concerning the bill before the Senate (S. 741), which included proposed definitions and a section on the designation of new animal drugs that were identical to those contained in the MUMS legislation enacted by Congress, stated the following:

> This definition incorporates the existing definition in the Code of Federal Regulations (21 CFR 514.1(d)(1)) with a further limitation to small numbers to assure that such intended uses will not be extended to a wider use. The Secretary is expected to further clarify this definition in regulations implementing this section. FDA is given broad latitude in determining what constitutes a minor use in a major species. The Congress intends for FDA to make the determination of minor use by evaluating, in the context of the drug development process, whether the incidence of the disease or condition occurs so infrequently that the sponsor of a drug intended for such use has no reasonable expectation of its sales generating sufficient revenues to offset the costs of development. The Congress does not intend for FDA to establish a test of commercial value, but rather directs FDA to determine whether the expected low use of a drug would discourage its development.

(S. Rept. 108–226 at 12–13.)

As is clear from the quoted discussion in the Senate report, Congress incorporated part of FDA's existing definition of "minor use" in § 514.1 (21 CFR 514.1) into the MUMS act definition of "minor use." In 1983 FDA issued a definition of "minor use" as part of regulations to provide for the agency's interpretation as to what data for minor use drugs would be sufficient to meet the current statutory standards (see 48 FR 1922, January 14, 1983). FDA's definition of "minor use" included use of drugs "in any animal species for the control of a disease that (*1*) occurs infrequently or (*2*) occurs in limited geographic areas" (§ 514.1(d)(1)(i)). Thus, minor use was previously only defined qualitatively by one of two factors that limited the size of the population needing treatment. The first limiting factor was that a disease occurred infrequently (i.e., rarely) in the total population of animals. FDA believes that the term "infrequently" includes both diseases or conditions that are uncommon in that they have a low but regular rate of occurrence over time in a given population and diseases or conditions that occur only sporadically as irregular outbreaks in a given population with a significantly higher rate of occurrence than normal when they occur and may not occur at all between outbreaks. The second limiting factor was that a disease or condition occurred in only a limited geographic area.

With the MUMS act, in respect to minor uses in major species, Congress added a "small number" limitation to both prongs of FDA's earlier definition: "an indication that occurs infrequently and in only a small number of animals or in limited geographical areas and in only a small number of animals annually" (21 U.S.C. 321(pp)). The Senate report indicates that the "small number" limitation added to both prongs was to ensure that the intended uses would not be "extended to a wider use." (S. Rept. 108–226 at 12). By doing

this, Congress not only required that the population of animals be limited by one of the two qualitative factors, but also required that, in either case, the population of animals affected must also meet the "small number" quantitative criteria. As a result, while some indications may be infrequent (because they are uncommon or occur only sporadically), they must also meet the requirement that they occur in only a small number of animals. Similarly, an indication may occur in a limited geographical area, but it must also occur in only a small number of animals annually. Congress defined "minor use" populations as limited to a "small number," but did not specify the small number(s), leaving it to the agency to further clarify the definition in this regard by regulation.

With respect to the term "infrequently," the Senate report states that FDA should determine whether the "incidence" of the disease "occurs so infrequently that the sponsor of a drug intended for such use has no reasonable expectation of its sales generating sufficient revenues to offset the costs of development" (S. Rept. 108–226 at 12–13). With respect to both prongs of the "minor use" definition, Congress did not intend FDA to establish a test of commercial value, but rather to determine "whether the expected low use of a drug would discourage its development" (S. Rept. 108–226 at 13). Consequently, FDA in these regulations has not established a dollar value or profit margin criterion in relation to "minor use."

The term "annually" only appears in the second prong of the statutory definition of "minor use" in connection with the small number of animals with the disease "in limited geographical areas." Thus, a minor use indication that occurs in a limited geographical area must also occur in a small number of animals annually. While "annually" does not apply to the first prong of the

definition of minor use, "infrequently and in only a small number of animals", FDA believes that for "a small numbers of animals" to have meaning, data on the number of animals in which the indication occurs must be considered over a period of time. FDA believes that to give effect to the statutory language, it is appropriate to annualize the data. For example, if a particular disease appears only once every 5 years, the number of animals may be relatively large, but when annualized, the disease may occur in only a "small number of animals." Looking at annualized numbers of affected animals is a reasonable approach under the "minor use" definition to considering whether there are sufficient drug development incentives in the absence of the MUMS incentives.

The term "limited geographical areas" is defined in proposed section 516.3(b)(4) as follows: "as used in the minor use definition, means regions of the United States distinguished by physical, chemical, or biological factors that limit the distribution of a disease or condition." If, for example, an area's mineral profile or moisture availability (chemical factors) can cause a medical condition directly (nutrient deficiency) or indirectly (suitable environment for specific parasites or bacteria), the case may be argued that the condition will only affect animals in that particular region. Chemical factors might also include possible environmental exposure to pesticides or other toxins used in a limited area. Physical factors such as altitude, proximity to salt or fresh water, or temperature can also influence the presence of parasites, vectors for parasites, as well as other microbes. These factors can also influence an animal's susceptibility to disease directly (high altitude disease) or indirectly if conditions cause stresses that weaken the immune system. Biological factors include the presence of vectors for disease, presence of toxic plants, and

inherent limitations of a species to live in a particular environment (e.g., saltwater versus freshwater fish).

As is clear from the minor use definition, geographic limitations alone will not be sufficient to make a particular intended use a minor use in a major species. The number of animals that live in a particular limited geographic area can still be very large. It was clearly the intent of Congress to limit the definition of minor use to a small number of animals and that is the intent of the definitions included in this proposed rule.

Small Number of Animals

The agency intends at some time in the future to propose that "small number of animals" be defined in regulations as a specific number for each of the seven major species. However, the number of animals that will provide the upper limit for the definition of "small number of animals" for each major species is, at this time, difficult to identify. Many factors need to be considered in establishing these numbers.

With respect to defining minor use, and by implication "small number of animals," Congress further noted in the Senate report (S. Rept. 108–226) accompanying the MUMS act that:

> FDA may initially make such determinations on a case-by-case basis. These initial determinations may form the basis for establishing or revising regulations which clarify the grounds or the process for determining whether a new animal drug is intended for a "minor use".

(S. Rept. 108–226 at 13).

Therefore, at this time, the agency is proposing only to clarify various other aspects of the current statutory definition of minor use, to gather further information to support the establishment of a "small number of animals" for

each major species, and to use the information currently available to make minor use determinations on a case-by-case basis. The agency particularly requests comment on the criteria it should use to determine the number that constitutes a "small number of animals" for each major species. Comments should clearly explain the rationale for any criteria suggested including economic, scientific, or other relevant factors. In an effort to stimulate comment and to increase the specificity of comments, the agency has summarized in the following paragraphs certain information it has considered to date regarding defining "small number of animals."

a. *Human orphan drugs as a model.* For human orphan drugs, the act provides that a disease or condition that affects less than 200,000 cases in the United States qualifies as a "rare disease or condition" (21 U.S.C. 360bb(a)(2)). As one approach to defining "small number of animals" for the purpose of implementing the MUMS act, the agency determined what percentage of the U.S. population of humans the number 200,000 represented when Congress enacted this meaning of "rare disease or condition." This calculation provided a figure of roughly 0.1 percent of the population. This percentage was then applied to populations of major species in the United States. Initial analysis indicated that using the 0.1 percent figure might be helpful with respect to dogs, cats, and horses. However, using this figure did not seem helpful for cattle, swine, chickens, and turkeys because the populations involved, the manner of drug use in those populations, and the drug development processes for those species are too dissimilar to the human drug scenario. Further analysis made clear that these factors were not sufficiently comparable for this approach to be viable, even for dogs, cats, and horses, and the approach was rejected.

While FDA recognizes classes of animals within species in the animal drug development process (examples include beef versus dairy cattle and broiler versus laying chickens), the diversity of these classes and the difficulty in determining whether a disease or condition might be unique to a class would make using these subpopulations of a species problematic in determining a maximum number of animals for a minor disease or condition. Therefore, using one maximum number would appear to be appropriate for animal species as well as humans, because for each major animal species the small number is intended to be a reflection of the market potential for a drug. It is immaterial whether that market potential exists because the disease or condition is relatively evenly distributed throughout the population or is largely confined to a particular age, gender, breed, or production class within that population. If the same number of animals is involved in each case, the market potential is essentially the same in each case. Therefore, one number appears to be appropriate as a means of determining the "small number" for a "minor use" for each of the seven species, regardless of subpopulations.

b. *Characterizing the population of animals affected by a disease or condition.* The human orphan drug maximum number for "rare disease or condition" is based on the prevalence of a disease or condition. That is the total number of people affected by the disease or condition at a given time. This differs from the incidence of a disease or condition, which is the number of new cases diagnosed over a period of time, e.g., the number of cases diagnosed per year. For several reasons, using prevalence of disease or condition is problematic for determining the number of animals for MUMS designation purposes.

In the case of cattle, swine, chickens, and turkeys, the number of animals affected with a given disease or condition at a given time does not take into account the fact that for animals like broiler chickens, the lifespan is so short that several flocks will go through the same facility in a year. Therefore, the number of birds potentially ill and/or treated over a year is much greater than the population that is ill on any given day. This suggests that the use of an incidence rate would be more appropriate in such cases.

However, incidence rates alone are also an imperfect descriptor even in the case of cattle, swine, chickens, and turkeys. The number of animals diagnosed with a disease or condition does not accurately reflect the number that will be administered a drug. For example, in the case of chickens, treatment of individual birds is impractical. When there is an outbreak of disease the entire flock is treated, including individuals with no signs of illness. In an attempt to limit minor use to a small number of animals, the way that drugs are actually administered should be taken into account. The number should refer to all birds administered a drug, not just to those clinically ill. This is significant for the determination of small number of animals because the actual size of the market is larger than the number of sick birds. A similar situation exists with respect to drugs intended for diagnosis or prevention of a disease or condition in major species. Such drugs will be subject to the same small number as those intended for treatment of a disease or condition.

Prevalence rates can be more appropriately used for horses, dogs, and cats because these animals' life spans typically exceed 1 year. Such animals are likely to be treated for chronic diseases over several years. These are added to newly diagnosed cases to provide the prevalence of the disease.

The number of humans diagnosed with a disease or condition (i.e., the prevalence of a disease in humans) is a close approximation of the number that will be treated for that disease or condition, if a treatment exists. For animals, there may be a very significant difference in the numbers of animals afflicted with a disease or condition and the number that will actually be diagnosed and treated. Many animals do not get regular veterinary care and, therefore, the probability of diagnosis is lower for animals than for humans. Furthermore, depending on the diagnosis, prognosis, and cost, a much higher percentage of animals will not be treated even after diagnosis.

Economic issues figure prominently in the calculation of the number of animals that will be treated for a disease or condition. In contrast to human medicine, there is essentially no third-party payment for animal drugs. Thus, cost for the treatment of animals is a major consideration. Because euthanasia is an option for animals, expensive or difficult treatment may be rejected by animal owners. On the other hand, because dogs, cats, and horses may be highly valued as "family members," the amount of money expended on individual animals of these species may far exceed that generally spent on individuals of the other major species of animals.

In the case of animals of agricultural importance, the decision to treat is based almost entirely on economic factors. In the case of chickens, where the profit margin is pennies per bird, it is often not worthwhile to treat.

It appears that for dogs, cats, and horses, the market potential for a drug at the time of its designation is reasonably represented by the total number of cases of the disease or condition estimated to exist over the course of a year at the time of a request for designation, taking into consideration that only a portion of the total affected population will actually be treated.

In the case of cattle, swine, chickens, and turkeys, the market potential for a drug at the time of its designation is reasonably represented by an estimation of the number of cases of a disease or condition that will occur in the total population of animals that will be alive over the course of a year at the time of a request for designation, taking into consideration that herd/flock treatment increases the number of animals administered a drug, and also taking into consideration that only a portion of the total affected population (and associated herd/flock mates) will actually be treated.

c. *Other information to be considered.* The agency is seeking information to help clarify three general issues with respect to each major animal species:

- The cost of drug development for a new chemical entity, adding an intended use for a new major species to a drug already approved for an intended use in another major species, and adding a new intended use to an existing approved drug for the same major species;
- The annual return on investment over a 7-year period necessary to stimulate the development of each of the previously mentioned costs; and
- The number of animals eligible to be administered the drug on an annual basis necessary to produce these returns on investment.

The information made available to FDA from all sources will be analyzed and used to establish the "small numbers of animals" for each major species needed to complete the clarification of the definition of minor use in major species. The agency reiterates its request for comment and solicits as much additional information as those commenting are willing to share regarding this issue. The FDA emphasizes that it is not now proposing a specific small number of animals for each major species, but is only proposing to establish such numbers in the future after it has collected additional information. In

the meantime, it is proposing to make such decisions on a case-by-case basis using the best information available at the time a decision is required.

3. Same Drug/Same Dosage Form/Same Intended Use

For a new animal drug to be eligible for designation under section 573 of the act, it must be intended for minor use or use in a minor species and must not be the same drug, in the same dosage form, for the same intended use as an animal drug already designated, conditionally approved, or approved. Therefore, the agency is also proposing to define "same drug," "same dosage form," and "same intended use" in proposed section 516.3.

a. *Same drug.* The first test of sameness to determine eligibility of an animal drug for designation is "same drug." The legislative history of the MUMS act in Senate Committee Report 108–226 states:

> The Secretary has discretion to define the term "same drug" as used in this section. In defining "same drug" the Secretary should take into account the purpose of this legislation to promote the development of minor use and minor species new animal drugs. A sponsor should be able to reap the benefits of designation only for products that are materially different from products that have already been approved, conditionally approved, or designated. So, for example, where two products differ only with respect to one or more inactive ingredients, they are the "same drug" for purposes of this section.

(S. Rept. 108–226 at 19).

The definition of "same drug" contained in this proposed rule is intended to give protection to the first conditionally-approved or approved MUMS-designated drug against a second sponsor's attempts to defeat exclusive marketing rights by introducing minor molecular changes. Because one goal of the MUMS act is to increase the availability of new animal drugs for minor

species and minor uses, a subsequent drug with minor chemical differences will be considered different only if the subsequent drug can be shown to be functionally superior to the first. The burden of proof is on the sponsor of the subsequent drug to demonstrate that its drug is safer or more effective in some way.

FDA is proposing this approach because it provides the best available mechanism to protect the integrity of marketing exclusivity, the chief incentive for MUMS drug development established by Congress, while allowing functionally superior drugs with similar chemical structure to be approved in a timely manner. This proposal is consistent with the human orphan drug regulations as codified in 21 CFR part 316 (see 21 CFR 316.3(b)(13)).

Functional superiority of a subsequent drug cannot be determined until the first drug is conditionally approved or approved because an unapproved drug has no labeled dosage and corresponding safety and effectiveness profile to which the challenger can be compared. Therefore, a sponsor of a subsequent drug with minor chemical differences from a MUMS-designated drug may not seek designation of the subsequent drug based on functional superiority until after the designated drug is conditionally approved or approved. If a drug is found to be functionally superior to a designated new animal drug after the designated drug is approved or conditionally approved, it will be considered a different drug and may be granted MUMS designation. After conditional approval or approval, it will enjoy its own 7-year period of exclusive marketing rights and the first drug's designation, conditional approval or approval, and period of exclusive marketing will remain in effect.

b. *Same dosage form.* The second test of sameness which the statute establishes to determine eligibility of an animal drug for designation is "same

dosage form." The agency proposes to use the long-established dosage form categories listed in Title 21 of the Code of Federal Regulations to implement this statutory requirement.

The categories follow: Oral dosage forms (21 CFR 520), implantation or injectable dosage forms (21 CFR 522), ophthalmic and topical dosage forms (21 CFR 524), intramammary dosage forms (21 CFR 526), miscellaneous dosage forms (21 CFR 529), and drugs in animal feeds (21 CFR 558).

Dosage forms that do not clearly fit within a specific category would fall within the miscellaneous category and the sameness of dosage form would be determined on a case-by-case basis. Drugs currently in the miscellaneous category include, for example, products administered by inhalation to terrestrial animals and products formulated for use by immersion of aquatic species. Although medicated animal feeds (i.e., drugs in animal feeds) have much in common with certain oral dosage forms, they are treated as a separate category because they are regulated quite differently. For example, drugs for use in animal feeds are subject to different manufacturing practices than other drugs and may not be used in an extralabel manner (21 CFR 530.11(b)). Thus, they are treated as separate dosage forms for purposes of implementing the MUMS act.

c. *Same intended use.* The third test of sameness which the statute establishes to determine the eligibility of an animal drug for designation is "same intended use." "Intended use" is defined in proposed 516.3(b)(11) for the purposes of subpart B of part 516 as "the intended treatment, control, or prevention of a disease or condition or the intention to affect the structure or function of the body of animals within an identified species, subpopulation of a species, or collection of species." Although this definition is generally

consistent with the manner in which the phrase has been used in the context of new animal drug approval, the definition proposed here is to be applied solely to the phrase "intended use" as it is used in these proposed regulations to determine whether two intended uses are the "same intended use" for purposes of qualifying for designation. It is not meant to define "intended use" in any other context. This interpretation of "intended use" for the purpose of designation is meant to protect the value of the exclusivity incentive provided by the statute. Because there can only be one designation for the "same drug," "same dosage form," and "same intended use," it is important that a minor difference in the intended use not permit a second sponsor to be granted designation for virtually the same product. For the purpose of new animal drug approval, it is important that every intended use to be included on the label be supported by data. Thus, the definition of "intended use" for purposes of designation reflects the need to protect product exclusivity.

Accordingly, the agency identified four basic principles for evaluating whether two intended uses represent the "same intended use." The first principle of "same intended use" establishes that whether two intended uses are considered the same, will not depend on whether exactly the same words are used to describe that intent on the labels of the products. Despite attempts over the years by FDA to increase the consistency of labeled intended uses (often also referred to as indications or claims), there remain many different ways to state the same intended use on a label. Differences in language alone do not necessarily result in different intended uses in the context of drug designation. For example, a disease or a causative organism may be known by several different names. The fact that two intended uses involve different

names for the same disease or causative organism does not cause the intended uses to be different.

The second principle of same intended use establishes that if one of the intended uses falls completely within the scope of the other, they are considered the same intended use for the purposes of designation. For example, an intended use for a particular disease or condition in all aquarium fish would include use for that disease or condition in black mollies (a type of aquarium fish) and, therefore, would be considered the same intended use for the same disease or condition in black mollies. Similarly, designation for black mollies would preclude a designation for all aquarium fish (but not a designation for all aquarium fish except black mollies).

This interpretation is driven by the marketing exclusivity provisions of the designation provision of the statute because marketing exclusivity for all aquarium fish includes exclusivity with respect to that intended use in all species within that designation.

The third principle of same intended use establishes that an intended use for a disease or condition caused by one (or a subset) of causative organisms is considered different from an intended use for the same disease or condition caused by a different causative organism (or subset of organisms) when the causative organisms involved can reliably be shown to be clinically significant causes of the disease or condition. For example, intended use for the treatment of pneumonia in cattle caused by *Pasteurella multocida* is not the same as intended use for the treatment of pneumonia in cattle caused by *Histophilus somni* (*Haemophilus somnus*).

The fourth principle of same intended use establishes that two intended uses that involve the same disease or condition but in different species, or

in different generally recognized subsets of the same species (such as production classes of food species), are not the same intended use. For example, an intended use for a particular disease or condition in growing turkeys is not the same as an intended use for the same disease or condition in laying turkeys.

B. Submission of Requests for Designation (Proposed § 516.14)

The agency proposes that all correspondence relating to a request for designation of a MUMS drug must be addressed to the Director, Office of Minor Use and Minor Species Animal Drug Development.

C. Eligibility to Request Designation (Proposed §§ 516.16 and 516.22)

The agency proposes that the person requesting designation must be the real party in interest of the development and the intended or actual production and sales of the drug because only this party can assure active pursuit of approval under section 512 or 571 of this act with due diligence required by section 573(a)(3)(B) of the act. In proposed § 516.22, the agency is proposing that foreign sponsors must have a permanent-resident U.S. agent to submit the request for designation so that the agency may assure that certain notifications (such as under section 573(c)(2)(A) of the act) and other communications with the sponsor are legally and effectively made.

D. Content and Format of a Request for MUMS-Drug Designation (Proposed § 516.20)

Proposed § 516.20 describes the content and format for a request for MUMS designation. Under proposed § 516.20, the request must be specific and must include certain information about the sponsor; a description of the proposed intended use for the drug; a description of the drug and dosage form;

a discussion of the scientific rationale for the intended use of the drug with reference to data; a specific description of the product development plan for the drug, its dosage form, and the intended use; if MUMS designation is based on a minor use, documentation that the proposed intended use is a minor use; a statement that the requestor is the real party in interest of the development and the intended or actual production and sales of the product; and a statement that the sponsor acknowledges that FDA will make certain information regarding the designation public. The information required to be included in a request for designation parallels that required for human orphan drug designation, but with some differences due to differences in the governing statutes and to differences between the health care practices for animals and humans in the United States.

For new animal drugs, each designation must be unique. That is, each designation is unique with respect to the drug and dosage form for use in the species or group of species for the treatment, control, or prevention of the disease or condition; or to affect the structure or function. This differs from the provisions of the human orphan drug legislation, which permits designation of multiple identical drugs prior to approval of any one of the drugs. The MUMS act facilitates the development of a broad range of animal drugs in part by discouraging multiple sponsors from pursuing identical uses.

Because each MUMS designation is unique in this way, it is important for the effective implementation of section 573(a)(2)(B) of the act that the initial designation of a drug be based on evidence that requesting sponsors clearly understand their responsibilities in terms of drug research and development and are prepared to accept those responsibilities. The most effective means of ensuring this is for the sponsor to work closely with the personnel in the

agency who will be responsible for reviewing the information submitted in support of the drug's conditional approval or approval. The parties should mutually agree that the scientific rationale for the drug is credible and that timely development of the drug in accordance with a drug development plan is possible. While not required, this is most effectively accomplished to the benefit of both the sponsor and the agency through the presubmission conference provisions of the investigational new animal drug (INAD) review process of the Center for Veterinary Medicine (CVM). Such presubmission conferences are held with members of CVM's Office of New Animal Drug Evaluation under the provisions of § 514.5 and may be held in person or via teleconference. The memorandum of conference that is created under the provisions of § 514.5(f) would suffice to document that the requirements of proposed § 516.20(b)(5) and (b)(6) have been met. Because a clear understanding by sponsors of agency approval requirements and the mutual development of a drug development plan to meet those requirements is so obviously beneficial to the effective utilization of resources by both parties, most new animal drug sponsors routinely follow this process and, therefore, for these sponsors, many of the requirements for submission of information under proposed § 516.20 to support designation would be met by reference to information routinely present in an INAD file.

Given the relatively limited return on investment associated with new animal drugs intended for minor uses or minor species, it is particularly critical, in keeping with the intent of the MUMS legislation, to enhance the availability of such drugs, that both sponsor and agency resources associated with MUMS drug development be used effectively and efficiently. The information proposed under § 516.20(b)(5) and (b)(6) as a condition of granting

a designation is essential for evaluation of a request for designation. Furthermore, as noted previously, the person requesting the designation must be the real party in interest of the development, production, and sale of the subject drug as proposed under § 516.20(b)(8). The information described in § 516.20(b)(1) through (b)(4) of the proposed rule is required to make the statutorily required determination under section 573(a)(2)(B) of the act that the drug requested for designation is not the same drug, in the same dosage form, for the same intended use as a drug already approved or conditionally approved. Proposed § 516.20(b)(7) and (b)(9) is similarly a reflection of specific requirements of the MUMS legislation.

E. Documentation of Minor Use Status (Proposed § 516.21)

Under proposed § 516.21, if the sponsor seeks MUMS-drug designation for a drug intended to be used as a minor use in a major species, the sponsor must include documentation that the use is limited to a small number of animals. Proposed § 516.21 details the documentation that is required.

The agency is proposing to define "intended use" of a drug and, more specifically, "same intended use" of a drug in these regulations. The primary discussion of these definitions can be found in section II.A.2.c of this document. It is important to reiterate here that this definition of intended use is to determine whether two intended uses are the "same intended use" for purposes of qualifying for designation; the definition is not directly applicable to the determination of whether a particular use in a major species is a minor use. As previously discussed, it is clear that Congress intended the agency's determination of whether a use is minor to depend upon the existence of a disease or condition in a major species that occurs in such a small number of animals that it would not warrant drug development in the absence of

special incentives. Thus, whether a use is a minor use in a major species is determined on the basis of the existence or occurrence of a disease or condition in the total population of a major species, and not by any population of animals that the sponsor may choose to define by the intended use or conditions of use that it places on its label.

Once the use of a drug for a given disease or condition is determined to be a minor use in a major species, a sponsor may establish an intended use for the product that represents only a subset of that minor use. That is, while a sponsor might be encouraged by the agency to develop the product for use in the entire population of animals comprising the minor use so that the drug would provide maximum benefit when used in accordance with its label, a sponsor generally may limit the intended use to only a portion of the eligible population. Marketing exclusivity will, however, be determined by the scope of the intended use on the label of the product.

Until the number for "small number of animals" for each major species has been formally established by regulation, a request for designation of a drug as a minor use in a major species needs to be supported by evidence that such intended use involves only a small number of animals of a major species as represented by the market associated with the potential population of animals to be administered the drug relative to the cost of drug development as discussed previously. Thus, such a request for designation must include information regarding the presence of the relevant disease or condition in the relevant major species on an annual basis, as well as information regarding the potential market represented by that number of animals relative to the development cost for the particular intended use being proposed.

The agency recognizes that such information is not readily available for uncommon animal diseases or conditions. Because there are no insurance records and national databases are lacking for diseases of animal species, except perhaps databases for diseases reportable because of their public health significance, it is difficult to determine verifiable numbers of cases for animal diseases or conditions on a National basis. Nevertheless, the agency understands that sponsors routinely do their own marketing research to determine the economic feasibility of pursuing any new animal drug approval.

As discussed previously, the number of concern with respect to minor use is the total number of animals that could potentially be administered a drug in association with the treatment, control, or prevention of a given disease or condition (annualized) taking into account that, for a variety of reasons, not all of those animals will actually be administered the drug.

Therefore, a sponsor needs to demonstrate through verifiable sources (surveys, literature, etc.) that the number of animals that could potentially be administered a drug in association with the treatment, control, or prevention of a given disease or condition (annualized) represents a market potential sufficient to support drug development with the added incentives of the MUMS act, but not without them.

A sponsor may request that the agency determine that the total population of animals that is affected by a particular disease or condition for which a MUMS drug is being considered for development should be decreased by the size of any subset of the total population to which administration of the drug can be demonstrated to be not medically justified. If such a demonstration can be made to the satisfaction of the agency, the remaining population of animals

affected by that disease or condition would be used to estimate the market potential for the drug.

A sponsor may demonstrate that administration is not medically justified in a subset of animals by, for example, referencing a consensus standard of practice established by an authoritative source that recommends against the administration of either the MUMS drug itself or drugs of the class of which the MUMS drug is a member to a subset of the population. In the absence of a consensus standard, the sponsor would need to provide reliable evidence that there is some attribute of the MUMS drug that renders its administration to the identified subset of animals not medically justified. A specific analysis of the relative risks and benefits of administering the MUMS drug to the subset of animals at issue, supported by all reliable information available to the sponsor, would be needed.

F. Timing of Requests for MUMS-Drug Designation (Proposed § 516.23)

In accordance with the requirement of section 573(a)(1) of the act, the agency is proposing that requests for designation of a new animal drug be accepted only prior to submission of a new animal drug application (NADA) for the drug under section 512 or 571 of the act.

G. Granting and Refusal to Grant MUMS-Drug Designation (Proposed §§ 516.24 and 516.25)

As required by sections 573(a)(2)(A) and (a)(2)(B) of the act, FDA proposes to refuse to grant a request for designation when the involved new animal drug is not intended for use in a minor species or for a minor use in a major species or the same drug in the same dosage form for the same intended use is already designated, conditionally approved, or approved. The agency is also proposing to refuse to grant a request for MUMS-drug designation if the request is found

to contain any untrue statement of a material fact, or to omit material information. As noted previously, the agency also proposes to refuse to grant designation if the request fails to contain a credible scientific rationale supporting the intended use, or fails to contain documentation sufficient to support an agency determination that successful drug development in a timely manner is possible.

H. Amendment to MUMS-Drug Designation (Proposed § 516.26)

The agency is proposing to allow sponsors to apply for amendments to MUMS-drug designation up to the time of approval of their marketing applications. The purpose of this proposal is to allow for situations in which testing data demonstrate that the proposed intended use is inappropriate due to unexpected issues of safety or effectiveness. This can occur when data demonstrate that the effectiveness of a drug in different populations or for different diseases or conditions differs from that for which the drug was initially designated. It can also occur when a group of species was originally designated, such as "all finfish" and it is subsequently discovered that the drug is not safe for use in a subset of fish species. The proposed intended use may have to be expanded or narrowed based on such unexpected findings. FDA would grant such an amendment request only if it found that the initial designation request was made in good faith and that the amendment is sought only to render the MUMS-drug designation consistent with unanticipated test results. If an amendment request for a minor use designation was to involve a new or expanded disease or condition and the number of animals affected would then exceed what would be considered a small number of animals annually, the amendment could not be granted.

I. Change in Sponsorship (Proposed § 516.27)

The agency proposes that the sponsor of a MUMS-designated drug may transfer sponsorship to another person. Such a transfer of sponsorship of the MUMS-designated drug will include transfer of the designation provided that this transfer of sponsorship is appropriately documented by both parties to the transfer and that the sponsor accepting the transfer certifies understanding of the responsibilities associated with developing or maintaining a MUMS-designated drug and demonstrates the capability of meeting those responsibilities as a condition of agency approval of the transfer.

Because MUMS-drug designations are unique and because the initial sponsor obtained designation after request and demonstration of capability to meet the requirements of section 573 of the act with respect to development and production of the designated drug, transfer of sponsorship of a MUMS-designated drug must depend upon a similar demonstration and agency approval.

J. Publication of MUMS-Drug Designations (Proposed § 516.28)

As required by section 573(a)(4) of the act, the agency will make public the designation and termination of designation of MUMS drugs. The agency proposes to meet this requirement by periodically updating a publicly available list of MUMS-designated drugs which would include basic identifying information regarding each MUMS drug on the list.

K. Termination of MUMS-Drug Designation (Proposed § 516.29)

The agency proposes to terminate designation of a MUMS drug on any of the grounds specified in section 573 of the act, or because the request is found to contain an untrue statement of material fact or to omit material

information, or because the agency withdraws approval of the application for the drug.

For the purposes of this proposed rule, the phrase "actively pursuing approval or conditional approval with due diligence" is intended to encompass a MUMS drug developer's good faith effort to pursue drug development and approval, or drug development, conditional approval, and subsequent approval, in a timely manner. Under proposed § 516.29(d), at a minimum, due diligence must be demonstrated by submission of annual progress reports in accordance with proposed § 516.30 that demonstrate the sponsor is progressing in accordance with the drug development plan submitted to the agency under proposed § 516.20 and by compliance with all applicable INAD requirements. However, FDA will consider the circumstances and may determine that other factors demonstrate an absence of due diligence.

L. Annual Reports for a MUMS-Designated Drug (Proposed § 516.30)

The agency proposes to require brief annual progress reports to the INAD file as one effective means of ensuring sponsor compliance with the requirement of section 573(a)(3)(B) of the act that new animal drug approval for a MUMS-designated drug be pursued with due diligence.

M. Exclusive Marketing Rights (Proposed §§ 516.31 and 516.34)

Under proposed § 516.34, the agency will send the sponsor of a conditionally-approved or approved MUMS-designated drug timely written notice recognizing exclusive marketing rights and make the same information publicly available by **Federal Register** publication. Under section 573(c)(1) of the act, FDA may not conditionally approve or approve another application for the same new animal drug, in the same dosage form, for the same intended use within 7 years after FDA has approved or conditionally approved a

designated MUMS drug. For this reason, no further action by FDA to bring about exclusive marketing rights is necessary. Proposed § 516.31 reflects the grounds for termination of designation and associated exclusive marketing rights established by section 573 of the act and discussed in association with proposed § 516.29 in section II.K of this document.

N. Insufficient Quantities of MUMS-Designated Drugs (Proposed § 516.36)

Proposed § 516.36 addresses situations where insufficient quantities of MUMS-designated drugs are being produced to meet demand. Under section 573(c)(2)(A) of the act, whenever the agency finds that a conditionally-approved or approved MUMS-designated drug sponsor cannot assure the availability of sufficient quantities of the drug to meet the needs of animals for which it was designated, the act provides that the agency may approve another application for the same drug in the same dosage form for the same intended use. Proposed § 516.36 provides a procedure whereby the agency would notify the approved MUMS-designated drug sponsor of the possible insufficiency of supply and would request, within a specified time, that the sponsor provide in writing information and data regarding how the sponsor can assure the availability of sufficient quantities of the drug, or consent to the approval of other marketing applications.

Following evaluation of the submitted information, the agency would issue an order with findings and conclusions, either reaffirming or terminating the MUMS-drug designation and the associated exclusive marketing rights. Any such order which the agency issues would constitute final agency action. In the event the agency's decision is to terminate the MUMS-drug designation and the associated exclusive marketing rights, FDA may approve any number of applications for the same drug, in the same dosage form, for the same

intended use, even if the additional sponsors cannot themselves assure the availability of sufficient quantities of the MUMS drug in question.

Once designation and exclusive marketing rights are terminated for failure to ensure the availability of adequate supplies, they cannot be restored even if the sponsor losing these privileges is later able to assure the availability of adequate supplies. It would be unreasonable to expect a second sponsor to invest in drug development to fill a gap if it could be shut out of the market at any time that the original sponsor could assure adequate supplies.

O. Availability for Public Disclosure of Data and Information in Requests and Applications (Proposed § 516.52)

Proposed § 516.52 provides rules for public disclosure of information. The agency recognizes that designation requests will contain confidential commercial information and, indeed, that the very existence of a MUMS-drug designation request may itself be confidential commercial information. In addition, a request for MUMS-drug designation is, in most instances, supported by information that will be incorporated into a sponsor's application for conditional approval or approval.

For all these reasons, proposed § 516.52(a) provides that unless previously publicly disclosed or acknowledged, FDA will not make public the existence of any pending MUMS-drug designation request prior to such time as FDA takes final action on the request. Proposed § 516.52(b) provides that, irrespective of whether the existence of a pending request for designation has been publicly disclosed or acknowledged, no data or information in the request are available for public disclosure.

Upon final FDA action on a request for designation, proposed § 516.52(c) provides that FDA will determine the public availability of data and

information in the designation request in accordance with part 20 (21 CFR part 20) and other applicable statutes and regulations. Under proposed § 516.52(d), via reference to proposed § 516.28, FDA will make a cumulative list of all MUMS-drug designations available to the public and update it periodically. Under proposed § 516.28, the list will contain the following information regarding each MUMS-designated drug: The name and address of the sponsor; the generic name and trade name, if any, of the drug; the date of granting MUMS-drug designation; the dosage form; and the species and intended use of the drug. In accordance with proposed § 516.29, FDA will give public notice of the termination of all MUMS-drug designations.

III. Conforming Changes

FDA is proposing to revise the definition of "sponsor" currently appearing in § 510.3 (21 CFR 510.3) to be consistent with the definition of "sponsor" proposed in the MUMS regulations in proposed § 516.3. The agency has recognized for some time that the scope of the definition in § 510.3 is overly narrow. It is inconsistent with one of the major subparts of part 510, Subpart G–Sponsors of Approved Applications, in failing to recognize that persons submitting and receiving approval for NADAs are also considered sponsors. The agency is taking this opportunity to resolve this long-standing inconsistency.

FDA is also proposing conforming changes in its regulations by removing § 514.1(d). The definitions under § 514.1(d)(1) were redefined by Congress in the MUMS act and are further clarified under proposed § 516.3. The provisions of § 514.1(d)(2) regarding the availability of guidance relating to MUMS drugs are now covered under FDA's good guidance practices in 21 CFR 10.115.

FDA also proposes to add a cross-reference to the MUMS designation records to 21 CFR 20.100, which lists regulations on the availability of specific categories of FDA records.

IV. Legal Authority

FDA's authority for issuing this proposed rule is provided by the Minor Use and Minor Species Animal Health Act of 2004 (21 U.S.C. 360ccc *et seq.*). When Congress passed the MUMS act, it directed FDA to publish implementing regulations (see 21 U.S.C. 360ccc note). In the context of the MUMS act, the statutory requirements of section 573 of the act, along with section 701(a) of the act (21 U.S.C. 371(a)) provide authority for this proposed rule. Section 701(a) authorizes the agency to issue regulations for the efficient enforcement of the act.

V. Analysis of Economic Impacts

FDA has examined the impacts of the proposed rule under Executive Order 12866, the Regulatory Flexibility Act (5 U.S.C. 601–612), and the Unfunded Mandates Reform Act of 1995 (Public Law 104–4). Executive Order 12866 directs agencies to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; and distributive impacts; and equity). The Regulatory Flexibility Act requires agencies to analyze regulatory options that would minimize any significant impact of a rule on small entities.

FDA tentatively finds that the proposed rule does not constitute an economically significant regulatory action as defined in 3(f)(1) of Executive Order 12866. We believe that the annual impacts will not exceed $100 million since by its very nature the rule applies to animal drugs that have a very small

market. Similarly, the administrative costs are unlikely to have a significant economic impact on a substantial number of small entities.

Section 202(a) of the Unfunded Mandates Reform Act of 1995 requires that agencies prepare a written statement, which includes an assessment of anticipated costs and benefits, before proposing any rule that may result in an annual expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of $100 million (adjusted annually for inflation) in any one year. The current threshold after adjustment for inflation is $115 million, using the most current (2003) Implicit Price Deflator for the Gross Domestic Product. FDA does not expect this proposed rule to result in any 1-year expenditure that would meet or exceed this amount. As such, no further analysis of anticipated costs and benefits is required by the Unfunded Mandates Reform Act of 1995.

The intention of this proposed rule, and therefore its benefit, is the creation of a system that would stimulate the development and marketing of animal drugs for rare diseases in major species and diseases found in minor species in the United States, which would otherwise not be economically viable under current market conditions. The countervailing cost, or risk of this proposed rule, would be the possibility of limited competition for approved drugs for a minor use drug indication or in a minor species drug due to the granting of the 7-year exclusive marketing right.

In addition to the benefit-risk tradeoff mentioned previously, there would be additional administrative costs for those companies seeking the MUMS designation for an NADA. We estimate that the designation request would require about 16 hours of preparation by a regulatory affairs official. At a benefit adjusted wage rate of almost $48 per hour for these employees, each

request would have administrative costs of about $760.[1] We estimate that about 15 separate sponsors would each annually submit, on average, 5 MUMS-designation requests. Administrative costs for these actions would total about $57,300.

The agency is also proposing in § 516.22 that foreign sponsors requesting designation, do so through a permanent-resident U.S. agent. This is consistent with the current requirements of § 514.1(a) because requests for MUMS designation will ultimately be submitted to an NADA file. The agency does not expect to receive many requests for designation from foreign sponsors, and estimates that number at less than one per year. As such, the agency has not quantified the cost of this provision but believes it would be negligible.

Amendments made to existing designations are expected to occur infrequently. We estimate that three amendments will be filed annually, requiring about 2 hours of preparation. At the same wage rate, this would cost an additional $300. Sponsors may also transfer sponsorship of a MUMS-designated drug or terminate the designation. We estimate that these activities would result in only 3 additional hours of administrative costs annually, totaling $150. The preparation of the annual report that would be required for each MUMS-designated drug is estimated to take about 2 hours. In the first year, this would result in another 150 hours of administrative costs, or about $7,200. FDA notifications to sponsors concerning insufficient quantities of approved MUMS-designated drugs are expected to be rare, about once each year. Sponsor responses are estimated to take 3 hours, for a cost of $150.

Assuming a sponsor chooses to seek the MUMS designation for its NADA, total administrative costs for this proposed rule are estimated at about $65,000

[1] 2000 National Industry-Specific Occupational Employment and Wage Estimates, U.S. Department of Labor, Bureau of Labor Statistics (*http://www.bls.gov/oes/2000/oesi3_283.htm*).

in the first year, and to increase each year thereafter due to the annual reporting requirements.

Regulatory Flexibility Analysis

1. Small Business Impacts

The Regulatory Flexibility Act requires agencies to prepare a regulatory flexibility analysis if a rule is expected to have a significant economic impact on a substantial number of small entities. Although we believe it is unlikely that significant economic impacts would occur, the following along with other sections of this preamble constitute the initial regulatory flexibility analysis.

One requirement of the Regulatory Flexibility Act is a succinct statement of any objectives of the rule. As stated previously in this analysis, with this proposed rule the agency intends to create a system, provided for by statute, that would stimulate the development and marketing of animal drugs for rare diseases in major species and diseases found in minor species in the United States, which would otherwise not be economically viable under current market conditions.

The Regulatory Flexibility Act also requires a description of the small entities that would be affected by the rule, and an estimate of the number of small entities to which the rule would apply. The Small Business Administration (SBA) defines the criteria for small businesses using the North American Industrial Classification System (NAICS). For pharmaceutical preparation manufacturers (NAICS number 325412), SBA defines small businesses as those with less than 750 employees. Census data shows that 723 companies with 901 establishments represent this category.[2] While about two-

[2] 2002 Economic Census, U.S. Census Bureau, Manufacturing Industry Series, Pharmaceutical Preparation Manufacturing, Table 4.

thirds of the establishments would be considered small using the SBA criteria, the agency acknowledges that many requests for MUMS designation would likely be received from multi-establishment companies that exceed the 750-employee limit on small businesses. Nonetheless, the cost of submitting a single request represents only about 0.1 percent of the revenues of the smallest set of establishments (those with one to four employees), and much smaller revenue percentages of all larger establishments. The agency believes that these costs would not represent a significant economic impact on these firms.

All of the costs described previously in this document would be incurred by any small business that applies for MUMS designation. These include costs for request preparation, amendments to designations, preparing annual reports, and responding to FDA notifications of insufficient quantities. The firms submitting requests for MUMS designation are expected to already have the necessary administrative personnel with the skills required to prepare the requests and fulfill reporting requirements as identified previously in this document.

2. Analysis of Alternatives

The Regulatory Flexibility Act requires that the agency consider any alternatives to the proposed rule that would accomplish the objective while minimizing significant impacts of the proposed rule. As stated previously, the agency believes that the proposed rule, due to the relatively small size of the costs, would not be likely to impose significant economic impacts on small businesses. As such, the agency believes the proposed rule achieves the objective with minimal costs to industry.

The statute that creates this system, Public Law 108–282, does not provide the agency a great deal of flexibility in the implementing regulations, such as

in determining the length of the exclusivity period or granting an exclusivity to more than one animal drug without regard to sameness of drug, dosage form, and intended use. The agency did consider, however, applying an explicit threshold number of animals of each major species as the upper bound of disease incidence in the definition of "minor use" of animal drugs. The agency determined that the data needed to develop these estimates would not be available in time for the publication date of this proposed rule as mandated by statute. The agency has therefore decided to address this issue in a later rulemaking, and instead consider the acceptability of each request for designation as a minor use animal drug on a case-by-case basis as provided for in the Senate report concerning the legislation.

VI. Paperwork Reduction Act of 1995

This proposed rule contains information collection provisions that are subject to review by the Office of Management and Budget (OMB), under the Paperwork reduction Act of 1995 (the PRA) (44 U.S.C. 3501–3520). A description of these provisions follows with an estimate of the annual reporting burden. Included in the estimate is the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing each collection of information.

FDA invites comments on these topics: (1) Whether the proposed collection of information is necessary for the proper performance of FDA's functions, including whether the information will have practical utility; (2) the accuracy of FDA's estimate of the burden of the proposed collection of information including the validity of the methodology and assumptions used; (3) ways to enhance the quality, utility, and clarity of the information to be collected; and (4) ways to minimize the burden of the collection of information

on respondents, including through the use of automated collection techniques and other forms of information technology.

Title: Designated New Animal Drugs for Minor Use and Minor Species 21 CFR Part 516

Description: The Minor Use and Minor Species (MUMS) Animal Health Act of 2004 amended the Federal Food, Drug, and Cosmetic Act (the act) to authorize FDA to establish new regulatory procedures intended to make more medications legally available to veterinarians and animal owners for the treatment of minor animal species as well as uncommon diseases in major animal species. This legislation provides incentives designed to help pharmaceutical companies overcome the financial burdens they face in providing limited-demand animal drugs. These incentives are only available to sponsors whose drugs are "MUMS-designated" by FDA. Minor use drugs are drugs for use in major species (cattle, horses, swine, chickens, turkeys, dogs, and cats) that are needed for diseases that occur in only a small number of animals either because they occur infrequently or in limited geographic areas. Minor species are all animals other than the major species, for example, zoo animals, ornamental fish, parrots, ferrets, and guinea pigs. Some animals of agricultural importance are also minor species. These include animals such as sheep, goats, catfish, and honeybees. Participation in the MUMS program is completely optional for drug sponsors so the associated paperwork only applies to those sponsors who request and are subsequently granted "MUMS designation." The proposed rule will specify the criteria and procedures for requesting MUMS designation as well as the annual reporting requirements for MUMS designees.

Under the proposed new part, § 516.20 provides requirements on the content and format of a request for MUMS-drug designation, § 516.26 provides requirements for amending MUMS-drug designation, provisions for change in sponsorship of MUMS-drug designation can be found under § 516.27, under § 516.29 are provisions for termination of MUMS-drug designation, under § 516.30 are requirements for annual reports from sponsor(s) of MUMS-designated drugs, and under § 516.36 are provisions for insufficient quantities of MUMS-designated drugs.

Description of Respondents: Pharmaceutical companies that sponsor new animal drugs.

FDA estimates the burden for this collection of information as follows:

TABLE 1.—ESTIMATED ANNUAL REPORTING BURDEN[1]

21 CFR Section	No. of Respondents	Annual Frequency per Response	Total Annual Responses	Hours per Response	Total Hours
516.20	15	5	75	16	1,200
516.26	3	1	3	2	6
516.27	1	1	1	1	1
516.29	2	1	2	1	2
516.30	15	5	75	2	150
516.36	1	1	1	3	3
Total					1,362

[1] There are no capital or operating and maintenance costs associated with this collection of information.

The burden estimate for this reporting requirement was derived in our Office of Minor Use and Minor Species Animal Drug Development by extrapolating the current INAD/NADA reporting requirements for similar actions by this same segment of the regulated industry and from previous interactions with the minor use/minor species community.

As required by section 3504(h) of the PRA, FDA has submitted a copy of this proposed rule to OMB for its review of these information collection provisions. Other organizations and individuals desiring to submit comments on the information collection requirements should send their comments to

OMB. Submit written comments on the information collection provisions to the Office of Information and Regulatory Affairs, Office of Management and Budget (OMB).

OMB is still experiencing significant delays in the regular mail, including first class and express mail, and messenger deliveries are not being accepted. To ensure that comments on the information collection are received, OMB recommends that written comments be faxed to the Office of Information and Regulatory Affairs, OMB, Attn: Fumie Yokota, Desk Officer for FDA, FAX: 202–395–6974.

VII. Environmental Impact

We have carefully considered the potential environmental impacts of this proposed rule and determined under 21 CFR 25.30(h) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment, nor an environmental impact statement is required.

VIII. Federalism

We have analyzed this proposed rule in accordance with the principles set forth in Executive Order 13132. We have determined that the proposed rule does not contain policies that have substantial direct effects on the States, on the relationship between the National Government and the States, or on the distribution of power and responsibilities among the various levels of government. Accordingly, we have tentatively concluded that the proposed rule does not contain policies that have federalism implications as defined in the Executive order and, consequently, a federalism summary impact statement has not been prepared.

IX. Comments

You may submit to the Division of Dockets Management (see **ADDRESSES**) written or electronic comments regarding this document. Please submit a single copy of electronic comments or two paper copies of any mailed comments, except that individuals may submit one paper copy. Identify your comments with the docket number found in brackets in the heading of this document. You may view received comments in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

List of Subjects

21 CFR part 20

Confidential business information, Courts, Freedom of information, Government employees.

21 CFR part 510

Administrative practice and procedure, Animal drugs, Labeling, Reporting and recordkeeping requirements.

21 CFR parts 514 and 516

Administrative practice and procedure, Animal drugs, Confidential business information, Reporting and recordkeeping requirements.

■ Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, it is proposed that 21 Chapter I be amended as follows:

PART 20—PUBLIC INFORMATION

■ 1. The authority citation for 21 CFR part 20 continues to read as follows:

Authority: 5 U.S.C. 552; 18 U.S.C. 1905; 19 U.S.C. 2531–2582; 21 U.S.C. 321–393, 1401–1403; 42 U.S.C. 241, 242, 242a, 242l, 242n, 243, 262, 263, 263b–263n, 264, 265, 300u–300u–5, 300aa–1.

■ 2. Amend § 20.100 by adding paragraph (c)(43) to read as follows:

§ 20.100 Applicability; cross-reference to other regulations.

* * * * *

(c) * * *

(43) Minor-use or minor-species (MUMS) drug designations, in § 516.52 of this chapter.

PART 510—NEW ANIMAL DRUGS

■ 3. The authority citation for 21 CFR part 510 continues to read as follows:

Authority: 21 U.S.C. 321, 331, 351, 352, 353, 360b, 371, 379e.

■ 4. Amend § 510.3 by revising paragraph (k) to read as follows:

§ 510.3 Definitions and interpretations.

* * * * *

(k) *Sponsor* means the person requesting designation for a minor-use or minor-species drug as defined in part 516 of this chapter, who must be the real party in interest of the development and the intended or actual production and sales of such drug (in this context, the sponsor may be an individual, partnership, organization, or association). *Sponsor* also means the person responsible for an investigation of a new animal drug. In this context, the sponsor may be an individual, partnership, corporation, or Government agency or may be a manufacturer, scientific institution, or an investigator regularly and lawfully engaged in the investigation of new animal drugs. *Sponsor* also means the person submitting or receiving approval for a new animal drug

application (in this context, the sponsor may be an individual, partnership, organization, or association). In all contexts, the sponsor is responsible for compliance with applicable provisions of the act and regulations.

PART 514—NEW ANIMAL DRUG APPLICATIONS

■ 5. The authority citation for 21 CFR part 514 continues to read as follows:

Authority: 21 U.S.C. 321, 331, 351, 352, 353, 360b, 371, 379e, 381.

§ 514.1 [Amended]

■ 6. Amend § 514.1 by removing paragraph (d).

■ 7. Add part 516 to read as follows:

PART 516—NEW ANIMAL DRUGS FOR MINOR USE AND MINOR SPECIES

Subpart A—General Provisions

Sec.

Subpart B—Designation of a Minor Use or Minor Species New Animal Drug

Sec.

Authority: 21 U.S.C. 360ccc–2, 371.

Subpart A—General Provisions

§ 516.1 Scope.

(a) This part implements section 573 of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 360ccc-2) and contains the following subparts:

(1) Subpart A—General Provisions.

(2) Subpart B—Designation of a Minor Use or Minor Species New Animal Drug.

(3) Subpart C—[Reserved]

(4) Subpart D—[Reserved]

(b) References in this part to regulatory sections of the Code of Federal Regulations are to Chapter I of Title 21, unless otherwise noted.

§ 516.2 Purpose.

This part establishes standards and procedures for implementing section 573 of the act, including designation of minor use or minor species new animal drugs and associated exclusive marketing rights.

§ 516.3 Definitions.

(a) The definitions and interpretations contained in section 201 of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 321) apply to those terms when used in this part.

(b) The following definitions of terms apply to all subparts of part 516:

Active moiety means the molecule or ion, excluding those appended portions of the molecule that cause the drug to be an ester, salt (including a salt with hydrogen or coordination bonds), or other noncovalent derivative (such as a complex, chelate, or clathrate) of the molecule, responsible for the pharmacological action of the drug substance.

Functionally superior means that a drug has been shown to provide a significant therapeutic or physiologic advantage over that provided by a conditionally-approved or approved MUMS drug, that is otherwise the same drug, in one or more of the following ways:

(i) The drug has been shown to be more effective, as assessed by effect on a clinically meaningful endpoint in adequate and well-controlled clinical trials, than a conditionally approved or approved MUMS drug, that is otherwise the same drug. Generally, this would represent the same kind of evidence needed to support a comparative effectiveness claim for two different drugs; in most cases, direct comparative clinical trials will be necessary; or

(ii) The drug has been shown to be safer than a conditionally-approved or approved MUMS drug, that is otherwise the same drug, in a substantial portion of the target population, for example, by the elimination of an ingredient or contaminant that is associated with relatively frequent adverse effects. In some cases, direct comparative clinical trials will be necessary.

Infrequently, as used in the minor use definition, means a disease or condition that is uncommon or that occurs only sporadically.

Limited geographical areas, as used in the minor use definition, means regions of the United States distinguished by physical, chemical, or biological factors that limit the distribution of a disease or condition.

Major species means cattle, horses, swine, chickens, turkeys, dogs, and cats.

Minor species means animals, other than humans, that are not major species.

Minor use means the intended use of a drug in a major species for an indication that occurs infrequently and in only a small number of animals or in limited geographical areas and in only a small number of animals annually.

MUMS drug means a new animal drug, as defined in section 201 of the act, intended for a minor use or for use in a minor species.

Same dosage form means the same as one of the dosage forms specified in the following parts of this chapter:

(i) Part 520: Oral dosage form new animal drugs (excluding use in animal feeds as specified in part 558 of this chapter).

(ii) Part 522: Implantation or injectable dosage form new animal drugs.

(iii) Part 524: Ophthalmic and topical dosage form new animal drugs.

(iv) Part 526: Intramammary dosage forms.

(v) Part 529: Certain other dosage form new animal drugs.

(vi) Part 558: New animal drugs for use in animal feeds.

Same drug means a MUMS drug for which designation, indexing, or conditional approval is sought that meets the following criteria:

(i) If it is a MUMS drug composed of small molecules and contains the same active moiety as a prior designated, conditionally-approved, or approved MUMS drug, even if the particular ester or salt (including a salt with hydrogen or coordination bonds) or other noncovalent derivative such as a complex, chelate or clathrate is not the same, it is considered the same drug; except that, if the prior MUMS drug is conditionally approved or approved and the second MUMS drug is shown to be functionally superior to the conditionally-approved or approved MUMS drug for the same intended use, it is not considered the same drug.

(ii) If it is a MUMS drug composed of large molecules (macromolecules) and contains the same principal molecular structural features (but not necessarily all of the same structural features) as a prior designated, conditionally-approved, or approved MUMS drug, it is considered the same drug; except that, if the prior MUMS drug is conditionally approved or approved and the second MUMS drug is shown to be functionally superior to the conditionally approved or approved MUMS drug for the same intended use, it is not considered the same drug. This criterion will be applied as follows to different kinds of macromolecules:

(A) Two protein drugs would be considered the same if the only differences in structure between them were due to post-translational events or infidelity of translation or transcription or were minor differences in amino acid sequence; other potentially important differences, such as different glycosylation patterns or different tertiary structures, would not cause the

drugs to be considered different unless the subsequent drug is shown to be functionally superior.

(B) Two polysaccharide drugs would be considered the same if they had identical saccharide repeating units, even if the number of units were to vary and even if there were postpolymerization modifications, unless the subsequent drug is shown to be functionally superior.

(C) Two polynucleotide drugs consisting of two or more distinct nucleotides would be considered the same if they had an identical sequence of purine and pyrimidine bases (or their derivatives) bound to an identical sugar backbone (ribose, deoxyribose, or modifications of these sugars), unless the subsequent drug is shown to be functionally superior.

(D) Closely related, complex partly definable drugs with similar pharmacologic intent would be considered the same unless the subsequent drug is shown to be functionally superior.

Same intended use means an intended use of a MUMS drug, for which designation, indexing, or conditional approval is sought, that is determined to be the same as (or not different from) a previously designated, conditionally-approved, or approved intended use of a MUMS drug. Same intended use is established by comparing two intended uses and not by simply comparing the specific language by means of which the intent is established in labeling in accordance with the following criteria:

(i) Two intended uses are considered the same if one of the intended uses falls completely within the scope of the other.

(ii) For intended uses associated with diseases or conditions with multiple causative organisms, two intended uses are not considered the same when they involve different causative organisms or different subsets of causative

organisms of that disease or condition when the causative organisms involved can reliably be shown to be clinically significant causes of the disease or condition.

(iii) Two intended uses of a drug are not considered the same if they involve different intended species or different definable subpopulations (including "production classes") of a species.

Sponsor means the person requesting designation for a MUMS drug who must be the real party in interest of the development and the intended or actual production and sales of such drug (in this context, the sponsor may be an individual, partnership, organization, or association). *Sponsor* also means the person responsible for an investigation of a new animal drug (in this context, the sponsor may be an individual, partnership, corporation, or Government agency or may be a manufacturer, scientific institution, or an investigator regularly and lawfully engaged in the investigation of new animal drugs). *Sponsor* also means the person submitting or receiving approval for a new animal drug application (in this context, the sponsor may be an individual, partnership, organization, or association). In all contexts, the sponsor is responsible for compliance with applicable provisions of the act and regulations.

Subpart B—Designation of a Minor Use or Minor Species New Animal Drug

§ 516.11 Scope of this subpart.

This subpart implements section 573 of the act. Specifically, this subpart sets forth the procedures and requirements for submissions to FDA of requests for designation of a new animal drug for a minor use or a minor species.

§ 516.12 Purpose.

This subpart establishes standards and procedures for determining eligibility for designation and the associated incentives and benefits described

in section 573 of the act, including a 7-year period of exclusive marketing rights.

§ 516.13 Definitions.

The following definitions of terms apply only in the context of subpart B of this part:

Director means the Director of the Office of Minor Use and Minor Species Animal Drug Development of the FDA Center for Veterinary Medicine.

Intended use means the intended treatment, control or prevention of a disease or condition, or the intention to affect the structure or function of the body of animals within an identified species, subpopulation of a species, or collection of species.

MUMS-designated drug means a new animal drug, as defined in section 201 of the act, intended for a minor use or for use in a minor species that has been designated under section 573 of the act.

MUMS-drug exclusive marketing rights or *exclusive marketing rights* means that, effective on the date of FDA conditional approval or approval as stated in the approval letter of an application for a MUMS-designated drug, no conditional approval or approval will be given to a subsequent application for the same drug, in the same dosage form, for the same intended use for 7 years, except as otherwise provided by law or in this subpart.

§ 516.14 Submission of requests for designation.

All correspondence relating to a request for designation of a MUMS drug must be addressed to the Director of the Office of Minor Use and Minor Species Animal Drug Development. Submissions not including all elements specified in § 516.20 will be returned to the sponsor without review.

§ 516.16 Eligibility to request designation.

The person requesting designation must be the sponsor and the real party in interest of the development and the intended or actual production and sales of the drug or the permanent-resident U.S. agent for such a sponsor.

§ 516.20 Content and format of a request for MUMS-drug designation.

(a) A sponsor that submits a request for designation of a new animal drug intended for a minor use or minor species must submit each request in the form and containing the information required in paragraph (b) of this section. While a request for designation may involve multiple intended uses, each request for designation must constitute a separate submission. A sponsor may request MUMS-drug designation of a previously unapproved drug, or a new intended use or dosage form for an already conditionally-approved or approved drug. Only one sponsor may receive MUMS-drug designation of the same drug, in the same dosage form, for the same intended use.

(b) A sponsor must submit two copies of a completed, dated, and signed request for designation that contains the following information:

(1) A request for designation of a new animal drug for a minor use or use in a minor species, which must be specific.

(2) The name and address of the sponsor; the name of the sponsor's primary contact person and/or permanent-resident U.S. agent including title, address, and telephone number; the generic and trade name, if any, of the drug; and the name and address of the source of the drug.

(3) A description of the proposed intended use for which the drug is being or will be investigated.

(4) A description of the drug and dosage form.

(5) A discussion of the scientific rationale for the intended use of the drug; specific reference, including date(s) of submission, to all data from nonclinical

laboratory studies, clinical investigations, copies of pertinent unpublished and published papers, and other relevant data that are available to the sponsor, whether positive, negative, or inconclusive.

(6) A specific description of the product development plan for the drug, its dosage form, and its intended use.

(7) If the drug is intended for a minor use in a major species, documentation in accordance with § 516.21, with appended authoritative references, to demonstrate that such use is a minor use.

(8) A statement that the sponsor submitting the request is the real party in interest of the development and the intended or actual production and sales of the product.

(9) A statement that the sponsor acknowledges that, upon granting a request for MUMS designation, FDA will make information regarding the designation publicly available as specified in § 516.28.

§ 516.21 Documentation of minor use status.

So that FDA can determine whether a drug qualifies for MUMS-drug designation as a minor use in a major species under section 573 of the act, the sponsor shall include in its request to FDA for MUMS-drug designation under § 516.20 documentation demonstrating that the use is limited to a small number of animals (annualized). This documentation must include the following information:

(a) The estimated total number of animals to which the drug could potentially be administered on an annual basis for the treatment, control, or prevention of the disease or condition for which the drug is being developed, including animals administered the drug as part of herd or flock treatment, together with a list of the sources (including dates of information provided and literature citations) for the estimate.

(b) If the drug is under development for only a subset of the estimated total number of animals to which the drug could potentially be administered on an annual basis for the treatment, control, or prevention of the disease or condition for which the drug is being developed, including animals administered the drug as part of herd or flock treatment, a demonstration that administration of the drug to animals other than the subset is not medically justified. The sponsor must also include a list of the sources (including dates of information provided and literature citations) for the justification that administration of the drug to animals other than the targeted subset is medically inappropriate.

(c) An estimate of the potential market associated with the total number of animals established in paragraph (a) of this section compared to an estimate of the development costs of the proposed drug, in the proposed dosage form, for the proposed intended use.

§ 516.22 Permanent-resident U.S. agent for foreign sponsor.

Every foreign sponsor that seeks MUMS-drug designation shall name a permanent resident of the United States as the sponsor's agent upon whom service of all processes, notices, orders, decisions, requirements, and other communications may be made on behalf of the sponsor. Notifications of changes in such agents or changes of address of agents should preferably be provided in advance, but not later than 60 days after the effective date of such changes. The permanent-resident U.S. agent may be an individual, firm, or domestic corporation and may represent any number of sponsors. The name and address of the permanent-resident U.S. agent shall be provided to the Director of the Office of Minor Use and Minor Species Animal Drug Development.

§ 516.23 Timing of requests for MUMS-drug designation.

A sponsor may request MUMS-drug designation at any time in the drug development process prior to the submission of an application for either conditional approval or approval of the MUMS drug for which designation is being requested.

§ 516.24 Granting MUMS-drug designation.

(a) FDA may grant the request for MUMS-drug designation if none of the reasons described in § 516.25 for refusal to grant such a request apply.

(b) When a request for MUMS-drug designation is granted, FDA will notify the sponsor in writing and will give public notice of the MUMS-drug designation in accordance with § 516.28.

§ 516.25 Refusal to grant MUMS-drug designation.

(a) FDA will refuse to grant a request for MUMS-drug designation if any of the following reasons apply:

(1) The drug is not intended for use in a minor species or FDA determines that there is insufficient evidence to demonstrate that the drug is intended for a minor use in a major species.

(2) The drug is the same drug in the same dosage form for the same intended use as one that already has a MUMS-drug designation but has not yet been conditionally approved or approved.

(3) The drug is the same drug in the same dosage form for the same intended use as one that is already conditionally approved or approved. A drug that FDA has found to be functionally superior is not considered the same drug as an already conditionally-approved or approved drug even if it is otherwise the same drug in the same dosage form for the same intended use.

(4) The sponsor has failed to provide:

(i) A credible scientific rationale in support of the intended use,

(ii) Sufficient information about the product development plan for the drug, its dosage form, and its intended use to establish that adherence to the plan can lead to successful drug development in a timely manner, and

(iii) Any other information required under § 516.20.

(b) FDA may refuse to grant a request for MUMS-drug designation if the request for designation contains an untrue statement of material fact or omits material information.

§ 516.26 Amendment to MUMS-drug designation.

(a) At any time prior to conditional approval or approval of an application for a MUMS-designated drug, the sponsor may apply for an amendment to the designated intended use if the proposed change is due to new and unexpected findings in research on the drug, information arising from FDA recommendations, or other unforeseen developments.

(b) FDA will grant the amendment if it finds:

(1) That the initial designation request was made in good faith;

(2) That the amendment is intended to make the MUMS-drug designated intended use conform to the results of new and unexpected findings in research on the drug, information arising from FDA recommendations, or other unforeseen developments; and

(3) In the case of a minor use, that as of the date of the submission of the amendment request, the amendment would not result in the intended use of the drug no longer being considered a minor use.

§ 516.27 Change in sponsorship.

(a) A sponsor may transfer sponsorship of a MUMS-designated drug to another person. A change of sponsorship will also transfer the designation status of the drug which will remain in effect for the new sponsor subject to the same conditions applicable to the former sponsor provided that at the time

of a potential transfer, the new and former sponsors submit the following information in writing and obtain permission from FDA:

(1) The former sponsor shall submit a letter to FDA that documents the transfer of sponsorship of the MUMS-designated drug. This letter shall specify the date of the transfer. The former sponsor shall also certify in writing to FDA that a complete copy of the request for MUMS-drug designation, including any amendments to the request, and correspondence relevant to the MUMS-drug designation, has been provided to the new sponsor.

(2) The new sponsor shall submit a letter or other document containing the following information:

(i) A statement accepting the MUMS-drug designated file or application;

(ii) The date that the change in sponsorship is intended to be effective;

(iii) A statement that the new sponsor has a complete copy of the request for MUMS-drug designation, including any amendments to the request and any correspondence relevant to the MUMS-drug designation;

(iv) A statement that the new sponsor understands and accepts the responsibilities of a sponsor of a MUMS-designated drug established elsewhere in this subpart;

(v) The name and address of a new primary contact person or permanent-resident U.S. agent; and

(vi) Evidence that the new sponsor is capable of actively pursuing approval with due diligence.

(b) No sponsor may relieve itself of responsibilities under the act or under this subpart by assigning rights to another person without:

(1) Assuring that the new sponsor will carry out such responsibilities; and

(2) Obtaining prior permission from FDA.

§ 516.28 Publication of MUMS-drug designations.

FDA will periodically update a publicly available list of MUMS-designated drugs. This list will be placed on file at the FDA Division of Dockets Management, and will contain the following information for each MUMS-designated drug:

(a) The name and address of the sponsor;

(b) The generic name and trade name, if any, of the drug;

(c) The dosage form of the drug;

(d) The species and the proposed intended use for which MUMS-drug designation was granted; and

(e) The date designation was granted.

§ 516.29 Termination of MUMS-drug designation.

(a) The sponsor of a MUMS-designated drug must notify FDA of any decision to discontinue active pursuit of conditional approval or approval of such MUMS drug. FDA must terminate the designation upon such notification.

(b) A conditionally-approved or approved MUMS-designated drug sponsor must notify the FDA at least 1 year before it intends to discontinue the manufacture of such MUMS drug. FDA must terminate designation upon such notification.

(c) MUMS designation shall terminate upon the expiration of any applicable period of exclusive marketing rights under this subpart.

(d) FDA may terminate designation if it independently determines that the sponsor is not actively pursuing conditional approval or approval with due diligence. At a minimum, due diligence must be demonstrated by:

(1) Submission of annual progress reports in a timely manner in accordance with § 516.30 that demonstrate that the sponsor is progressing in

accordance with the drug development plan submitted to the agency under § 516.20 and

(2) Compliance with all applicable requirements of part 511 of this chapter.

(e) Designation of a conditionally-approved or approved MUMS-designated drug and the associated exclusive marketing rights may be terminated if the sponsor is unable to provide sufficient quantities of the drug to meet the needs for which it is designated.

(f) FDA may also terminate MUMS-drug designation for any drug if the agency finds that:

(1) The request for designation contained an untrue statement of material fact; or

(2) The request for designation omitted material information required by this subpart; or

(3) FDA subsequently finds that the drug in fact had not been eligible for MUMS-drug designation at the time of submission of the request;

(4) The same drug, in the same dosage form, for the same intended use becomes conditionally approved or approved for another sponsor; or

(5) FDA withdraws the conditional approval or approval of the application for the new animal drug.

(g) For a conditionally-approved or approved drug, termination of MUMS-drug designation also terminates the sponsor's exclusive marketing rights for the drug but does not withdraw the conditional approval or approval of the drug's application.

(h) Where a drug has been MUMS-designated for a minor use in a major species, its designation will not be terminated on the grounds that the number of animals to which the drug could potentially be administered on an annual

basis for the treatment, control, or prevention of the disease or condition for which the drug is being developed, including animals administered the drug as part of herd or flock treatment, subsequently increases.

(i) When a MUMS-drug designation is terminated, FDA will notify the sponsor in writing and will give public notice of the termination of the MUMS-drug designation.

§ 516.30 Annual reports for a MUMS-designated drug.

Within 14 months after the date on which a MUMS drug is granted designation and annually thereafter until approval, the sponsor of a MUMS-designated drug shall submit a brief progress report on the drug to the investigational new animal drug file addressed to the Director of the Office of Minor Use and Minor Species Animal Drug Development that includes the following information:

(a) A short account of the progress of drug development including a description of studies initiated, ongoing, and completed, and a short summary of the status or results of such studies;

(b) A description of the investigational plan for the coming year, as well as any anticipated difficulties in development, testing, and marketing; and

(c) A brief discussion of any changes that may affect the MUMS-designated drug status of the product. For example, situations in which testing data demonstrate that the proposed intended use is inappropriate due to unexpected issues of safety or effectiveness.

§ 516.31 Scope of MUMS-drug exclusive marketing rights.

(a) After conditional approval or approval of an application for a MUMS-designated drug in the dosage form and for the intended use for which MUMS-drug designation has been granted, FDA will not conditionally approve or approve another application or abbreviated application for the same drug in

the same dosage form for the same intended use before the expiration of 7 years after the date of conditional approval or approval as stated in the approval letter from FDA, except that such an application can be conditionally approved or approved sooner if, and at such time as, any of the following occurs:

(1) FDA terminates the MUMS-drug designation and associated exclusive marketing rights under § 516.29; or

(2) FDA withdraws or proposes to withdraw the conditional approval or approval of the application for the drug for any reason; or

(3) The sponsor with exclusive marketing rights provides written consent to FDA to conditionally approve or approve another application before the expiration of 7 years; or

(4) The sponsor fails to assure a sufficient quantity of the drug in accordance with section 573 of the act and § 516.36.

(b) If an application for a MUMS drug cannot be approved until the expiration of the period of exclusive marketing of a MUMS-designated drug, FDA will so notify the sponsor in writing.

§ 516.34 FDA recognition of exclusive marketing rights.

(a) FDA will send the sponsor (or the permanent-resident U.S. agent, if applicable) timely written notice recognizing exclusive marketing rights when an application for a MUMS-designated drug has been conditionally approved or approved. The written notice will inform the sponsor of the requirements for maintaining MUMS-designated drug exclusive marketing rights for the full 7-year term. This notice will generally be contained in the letter conditionally approving or approving the application.

(b) When an application is conditionally approved or approved for a MUMS-designated drug that qualifies for exclusive marketing rights, FDA will

publish this information in the **Federal Register** at the time of the conditional approval or approval. This notice will generally be contained in the notice of conditional approval or approval of the application.

§ 516.36 Insufficient quantities of MUMS-designated drugs.

(a) Under section 573 of the act, whenever the FDA has reason to believe that sufficient quantities of a conditionally-approved or approved, MUMS-designated drug to meet the needs for which the drug was designated cannot be assured by the sponsor, the FDA will so notify the sponsor of this possible insufficiency and will offer the sponsor the following options, one of which must be exercised by a time that FDA specifies:

(1) Provide FDA information and data regarding how the sponsor can assure the availability of sufficient quantities of the MUMS-designated drug within a reasonable time to meet the needs for which the drug was designated; or

(2) Provide FDA in writing the sponsor's consent for the conditional approval or approval of other applications for the same drug before the expiration of the 7-year period of exclusive marketing rights.

(b) If, within the time that FDA specifies, the sponsor fails to consent to the conditional approval or approval of other applications and if FDA finds that the sponsor has not shown that it can assure the availability of sufficient quantities of the MUMS-designated drug to meet the needs for which the drug was designated, FDA will issue a written order terminating designation of the MUMS drug and the associated exclusive marketing rights. This order will state FDA's findings and conclusions and will constitute final agency action. An order terminating designation and associated exclusive marketing rights may issue whether or not there are other sponsors that can assure the

availability of alternative sources of supply. Such an order will not withdraw the conditional approval or approval of an application. Once terminated under this section, neither designation, nor exclusive marketing rights may be reinstated.

§ 516.52 Availability for public disclosure of data and information in requests.

(a) FDA will not publicly disclose the existence of a request for MUMS-drug designation under section 573 of the act prior to final FDA action on the request unless the existence of the request has been previously publicly disclosed or acknowledged.

(b) Whether or not the existence of a pending request for designation has been publicly disclosed or acknowledged, no data or information in the request are available for public disclosure prior to final FDA action on the request.

(c) Except as provided in paragraph (d) of this section, upon final FDA action on a request for designation, the public availability of data and information in the request will be determined in accordance with part 20 of this chapter and other applicable statutes and regulations.

(d) In accordance with § 516.28, FDA will make a cumulative list of all MUMS-drug designations available to the public and update such list periodically. In accordance with § 516.29, FDA will give public notice of the termination of all MUMS-drug designations.

Subpart C—[Reserved]

Subpart D—[Reserved]

Dated: 8/31/05

August 31, 2005.

Jeffrey Shuren,
Assistant Commissioner for Policy.

[FR Doc. 05–????? Filed ??–??–05; 8:45 am]

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